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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/591,087	MONSAN ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-33 and 36-40* is/are pending in the application.

4a) Of the above claim(s) *21-24,27-30 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-20, 25-26, 31-33 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/21/09 has been entered.

Status of Claims

Claims 19-33 and 36-40 are pending in the application.

Claims 21-24, 27-30 and 36 are withdrawn from further consideration.

Claims 1-18 and 34-35 are cancelled.

Claims 19-20, 25-26, 31-33 and 37-40 are under examination.

Withdrawn Objection/Rejection

In view of the amendments to the claims and applicants' arguments the 35 USC 112, second paragraph has been withdrawn.

Claim Objections

Claim 19, as amended, is objected to because of the following informalities: grammatical error in claim 19, step c)

of a medium containing "either" at least one substrate.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-20, 25-26, 31-33 and 37-38, as amended, and newly added claims 39-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter Rejection

A). Claim 19 which recites a "first" minimum medium containing either at least one substrate and a "second" minimum medium are not supported in the as-filed specification. The original disclosure does not describe the differentiating/characterizing features of these media. The Examples e.g., Example 1 describe species of the media M9 but

not a first and second media. Furthermore, there is no description of what constitutes a M9 medium. Thus, at the time of applicants' filing the broad scope of the claim any first and second medium for any substrate or product is not disclosed or even contemplated in the as-filed specification. Consequently, the as-filed specification does describe e.g., claim 1 step c) testing in parallel the growth **capacity** of the population of transformed host cells on a **first** and **second** media.

Applicants pointed out the alleged support at e.g. pages 6-10 of the instant disclosure. However a review of these cited sections do not reveal a first or second medium or growth capacity but defines only the numerical range for A(i) as 1-100.

[This rejection can be obviated if applicants can point out where in the as-filed specification specific support can be found for the new claim limitations.]

Written Description Rejection

The specification fails to provide an adequate written description of the claim method of testing in parallel the growth capacity of the population of transformed host cells on a first minimum medium containing either at least one substrate {Ai}, as the only source of an element essential to growth and on a second minimum medium containing said product {B} as the only source of an element essential to growth. There is no

description in the specification as to a first medium that is specifically attributed to the substrate (Ai) medium and the second medium specifically to the product (B) medium. There are no differentiating features of the two media. The detail description in the specification, e.g., Example 1 describes species of the media, M9 as applied to a species of substrate/product. The genus claim to a first and second media provides for no definite composition of any media. The claim to a media of undefined composition coupled with any kind of substrate/product covers a limitless number of media apply to any substrate or product. The detail description to a species is inadequate for the genus claim. The law clearly indicates that a patent specification must describe the claimed invention in sufficient detail (not in general terms). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures and formulas to show that the invention is complete. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQM 1961, 1966 (Fed. Cir. 1997); MPEP 2163. The general statements in the specification are therefore not a detail description of the invention. A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise

definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993.

Applicant, at the time of filing, is deemed to have not invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). [Amending the claim to recite the specific substrate/product with a media use for the substrate/product species would obviate this rejection. See for example, the Examples.]

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-20, 25-26, 31-33 and 37-38, as amended, and newly added claims 39-40 are rejected under 35 U.S.C. 112, second

paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. In claim 19, step c), it is vague and indefinite as to the parallel testing of a first and second media of the population of transformed host cells containing Ai or B. It is unclear as to how the parallel testing of the transformed cells is accomplished both in the two different Ai medium and B medium, especially in the absence of positive support in the original disclosure.

2. Claim 19 is vague and indefinite as to whether growth capacity refers to the amount of transformed host cells being parallel tested in either medium or to the ability of the transformed host cells to grow in two separate medium.

3. Claim 19 is vague and indefinite as to the differentiating features of the first and second minimum medium or the essential element in Ai or B. The metes and bounds of each of the media are not clearly set forth in the claim or specification.

4. Claim 20 is indefinite and inconsistent with claim 20 in the recitation of a "minimum medium". The base claim 19 recites for a first and second minimum media. It is unclear which of the first and second minimum media the broader minimum medium of

claim 20 refers to or if this media is different from the first and second media for Ai and B of claim 19.

5. The term "high GC" in claim 39 is a relative term which renders the claim indefinite. The term "high" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to the basis by which a library of sequences is considered to be of high GC content one over the other of either the member in a library or the library per se.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-20, 25-26, 31-33 and 37-38, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Hoch (USP 6,368,793).

For claims 19-20, 25-26, 31-33 and 37-38, Hoch discloses throughout the patent at e.g., col.1, line 34 up to col. 3, line 64; a process to identify the metabolic pathway from a

source compound(Ai as claimed) to a target compound(B) that involves the creation/identification of an easily genetically-manipulatable organism containing an inducible signal, which is activated when a target compound is metabolized. This is followed by the screening of nucleic acid in the organism to identify genes which metabolize the source compound to the target compound. FIG. 11, for example, describes a method comprising selection of microbial isolates that are capable of metabolizing a target compound "T" (B, as claim), but not a source compound "S"(Ai, as claim), to an essential factor(element as claimed). Essential factors include elements like carbon. In a second step, the pathway responsible for the catabolism of compound "T" is identified and made conditional. That is, the gene(s) for the pathway is cloned and placed under control of an inducible promoter such that growth on the target compound is turned "ON" only when the inducer is present. This engineered strain is referred to as the "tester strain". The third part of the method is the transfer of foreign DNA from environmental sources into the tester strain, followed by selection for growth on the source compound "S" in the presence of inducer. Such positive clones either are capable of metabolizing compound

"S" in the absence of inducer, in which case utilization of "S" does not require prior conversion to compound "T" (FIG. 11; pathway I), or alternatively metabolize compound "S" only when "T" catabolism is "ON", suggesting that utilization of "S" proceeds via compound "T" to intermediary metabolism (FIG. 11; pathway II) (step c, as claim). These latter clones are further analyzed and the biocatalysts for the conversion of "S" to "T" are characterized. A specific embodiment of the metabolic selection strategy is shown in FIG. 12, where "S" is 2-keto-L-gulonate (2-KLG), and "T" is ascorbic acid (AsA) which can be metabolized to carbon and energy.

For claim 19, step c) Hoch discloses that screening refers to methods for identifying a nucleic acid sequence of interest from among hundreds or thousands. Screening may include classical selection, where typically the phenotype to be identified is growth on selective media (reads on first and second media). Selective media is meant on which the host strain will not grow or grows poorly, but that strains with the nucleic acid of interest will grow in a manner which can be readily distinguished from host strain growth by methods well-known in the art. Growth in the absence of the inducer indicates that metabolism of the

source compound to the essential element or factor does not require prior conversion to the target compound, rather it may proceed directly, or through an intermediate, to the essential element or factor. Samples from diverse natural environments were collected to use for the isolation of microbes that can utilize ascorbic acid (AsA) as the sole carbon source.

Claims 19-20, 25-26, 31-33 and 37-38, as amended, and new claims 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoch et al (2003/0068807A1)

For claims 19-20, 25-26, 31-33 and 37-40; Hoch et al discloses at e.g., paragraph [0011] methods of identifying a host cell that encodes a metabolic pathway that converts a precursor molecule into a desired product compound, where steps (a) and (b) are optional, by (a) culturing a population of host cells under conditions that allow expression of the metabolic pathway; (b) assaying the host cells, or extract thereof, for the presence of the desired product compound; and (c) identifying a host cell that contains the desired product compound in the presence, but not in the absence, of the precursor molecule; where an identified host cell from step (c) contains a metabolic pathway that converts the precursor

molecule into a desired product compound. A library of expressible nucleic acid molecules is introduced into the population of host cells prior to step (a). The nucleic acid molecules are derived from an environmental source, such as mud, soil. The host cell is a bacterial cell and can be derived from an environmental source. The precursor molecule is e.g., 7-aminocephalosporanic acid (7-ACA).

For claim 25, Hoch et al discloses at e.g., paragraph [0016] that organisms can be identified that contain enzymatic pathways that convert precursor molecules into active compounds. The genes that encode the conversion pathways can be cloned. Alternatively or additionally, methods can be used to isolate and characterize these active compounds from the organism or recombinant organism.

For claims 32-33 and 37-38; Hoch discloses at e.g., paragraph [0025] that host cell mean a cell with a metabolic pathway that converts a precursor molecule to a desired product compound. A host cell can be, for example, a bacterial cell. In addition, a host cell can be a cell that is non-culturable, or is not easily cultured, in the laboratory as well as cells that are culturable. For example, DNA can be extracted from a non-culturable cell from an environmental source and this DNA can be

used to generate a library in a culturable organism. When a library of expressible nucleic acids is introduced into the host cell, it is understood that the host cell is able to be transformed or transfected with genetic material.

For claim 40, Hoch discloses at e.g., paragraph [0039] expression constructs introduced into the appropriate library host organisms. A variety of methods can be used, which include, for example, transformation and transfection. Exemplary prokaryotic library host organisms can include, for example, Streptomyces lividans. After the library host cells containing expression constructs are pooled to form a library, they can be optionally amplified by techniques known in the art.(The claim high GC content is inherent to Streptomyces lividans. See instant specification admission at e.g., page 27, line 23.)

Applicant cannot rely upon the French foreign priority papers filed on 3/23/04 to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

[Please note should applicants provide a translation of the French priority papers, the rejection will be maintained under the appropriate 35 USC 102(e) and 102(a).]

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 19-20, 25-26, 31-33 and 37-38, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Handelsman et al (USP 7008767) in view of Hoch (USP 6368793) for reasons of record as reiterated below.

Handelsman discloses throughout the patent at e.g., col. 2, line 9 up to col. 4, line 45, including the drawings:

> .. [A] method [that] provides host cells which have been engineered to express the opening reading frames of genomic DNA sub-cloned from a heterologous microorganism. The subject method detects changes in the phenotype of the host cell which are dependent on expression of open reading frames from the genomic DNA….
>
> …A method for identifying non-proteinaceous compounds produced by a uncultivated microorganisms, comprising i) generating a library of host microorganism(populations of cells, as claimed in claim 19) transfected with a variegated population of vectors containing genomic DNA isolated from a sample of uncultivated microrganisms, which genomic DNA includes open reading frame (ORF) sequences which can be expressed from the vector in the host microorganism; ii) culturing the transfected host microorganism under conditions wherein the ORFs are expressed; iii) detecting ectopic production of non-proteinaceous compounds by the host microorganisms.
>
> FIG. 1: pBeloBAC11 vector(reads on library of nucleic acid of claim 19).

FIG. 3: is a table illustrating the average size inserts in various BAC libraries described in the art.

FIG. 5: is a table describing the phenotypes conferred on the host cell by the expression of the Bacillus cereus BAC library.

Handlesman discloses the variegated population of cells at e.g., col. 9, line 64 up to col. 10, line 3 and col. 21, line 65 up to col. 22, line 59.

Handelsman further discloses at e.g., col. 30, line 49 up to col. 31, line 40:

A High-Throughput Robotic Screening of BAC Clones for Production of Natural Products:

The high throughput processing and analysis of large genomic libraries by the subject method can be automated, e.g., using automated/robotic systems. The automation can include activities as: 1) arraying and storage of BAC libraries; 2) growth and separation of cells/conditioned culture media; and 3) testing conditioned media in biological and biochemical assays. These are outlined below for the exemplary embodiment of a BAC genomic DNA library. The detailed methodologies will vary from one embodiment to the next, but can be readily implemented by those skilled in the art.

High throughput assays: The conditioned media can be tested for activity in high throughput biochemical or biological assays adapted for automated readouts…the method can employ established procedures for robotic antimicrobial testing. In general, such assays are performed in multi-well plates or by placing small aliquots of conditioned media onto plates seeded with a bacterial…lawn….In addition to antimicrobial assays, as described above the culture supernatants can be tested in biochemical assays, as.... whole cell assays, e.g., which detect changes in phenotype dependent on addition of conditioned media. To increase throughput, it may be desirable to test pools of culture supernatants….

See the Examples for a detail description of the method.

Handelsman does not disclose that the only source of an element essential to growth is either the substrates or the product produced by the biosynthetic pathway. However, Hoch discloses throughout the patent at e.g., col.1, line 34 up to col. 3, line 64:

> An example of a selection strategy which can be used to identify the metabolic pathway from a source compound to a target compound is diagrammed in FIG. 11. As a first step, microbial isolates are selected that are capable of metabolizing a target compound "T", but not a source compound "S", to an essential factor. Essential factors can include elements like carbon……..
>
> Growth in the absence of the inducer indicates that metabolism of the source compound to the essential element or factor does not require prior conversion to the target compound, rather it may proceed directly, or through an intermediate, to the essential element or factor….
>
> Alternatively, if the intermediate is freely interconvertable with the desired target compound as well as to the essential element, growth in the absence of the inducer may be an acceptable outcome, or even desirable. By "freely interconvertable" is meant that an enzymatic pathway is present to allow the intermediate to be converted to the target. The interconvertability of the compounds would also be determined using the methods described above for obtaining a pathway directly to the target compound.
>
> Samples from diverse natural environments were collected to use for the isolation of microbes that can utilize ascorbic acid (AsA) as the sole carbon source. No bacterial species has previously been reported to grow on AsA minimal medium.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to test in the method of Handelsman the substrate or product by the

growth of said product or substrate as taught by Hoch. There would be a reasonable expectation of success in measuring the growth of the product since Hoch has extensively discussed the conditions by which the growth can be tested or measured. Thus the test of products or substrates based on its growth is a predictable result as the conventionality of said test is taught by Hoch, supra.

If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d.

Response to Arguments

Applicants argue that that "a library of sequences of nucleic acid", as claimed in the present invention, is completely different from "a library of host microorganisms" in Handelsman et al.

In reply, Handlesman teaches both a library of sequences derived from metagenomic library and library of host microorganisms. Attention is drawn to col.2 up to col. 4, above:

> …A method for identifying a product of a biosynthetic pathway, comprising i) providing host cells containing a replicable vector including genomic DNA isolated from a source of uncultivated microorganisms, which host cells are provided under conditions wherein expression of open reading frame sequence(s) of the genomic DNA occurs….

Applicants further note that Handelsman et al. differs from the claimed invention as Handelsman et al. simply relates to the detection of gene products by comparing gene products of transfected host cells to that of non-transfected host cells (Handelsman et al. specification at column 2, lines 43-50). However, there is neither explicit nor implicit teaching of any method in Handelsman et al., which allows determining the transformation of a desired product from one or more substrate(s) as is claimed in the present invention. Indeed, the Office Action points to no teaching in Handelsman regarding the culturing of a transfected host cell on a first minimum medium containing at least one substrate and a second minimum medium containing a chosen product.

In response, the comparison of gene products of the trsnfected host cell to the non-transfected host cell would implicitly indicate testing by growth of the product and/or tranformation of the source (substrate) to the product. Such determination, either of the product growth or both the substrate and product is a process well within the ordinary

skill in the art to determine. Attention is drawn to Handelsman above which states:

> ….[A] method for identifying a product of a biosynthetic pathway, comprising i) providing host cells containing a replicable vector including genomic DNA isolated from a source of uncultivated microorganisms which host cells are provided under conditions wherein expression of open reading frame sequence(s) of the genomic DNA occurs; and ii) detecting a compound produced by the host cells, e.g., relative to host cells lacking the genomic DNA.

Furthermore, Handelsman discloses at col. 29, lines 46-49, the detection step of parallel testing to detect a phenotypic change in the host cell which is induced by products of the expression of the heterologous genomic sequences. The growth is done in deep-well 96-well plates (or multi well) (known in the art as parallel testing). See further the high throughput (HT) assay disclose by Handelsman above.

Applicants state that Handelsman et al. is completely silent on the detection method of parallel testing in the present invention, where host cells are selected on a medium containing at least one substrate as the only source of an element essential to growth, and at the same time, on a separate medium containing the product as the only source of an element essential to growth. In the present invention, testing cells on a medium containing substrate {Ai} allows selection of cells

capable of metabolizing substrate {Ai}; while simultaneous testing cells on a separate medium containing product {B} enables selection of cells capable of using {B} for growth. This confers a clear advantage.

In reply, as stated above Handelsman teaches HT assay which will suggest the parallel testing of transformed host cells to determine whether the transformed host cells contain the substrate and/or transformed into the desired product. This is not a clear advantage. Rather, an unexpected advantage the determination of which is well known in the art. Obviously, one can determine the presence of either the substrate or the product or both to determine whether the substrate has been converted by the metabolic pathway to the desired product or not. Side reactions, normally kept to minimum, are expected and not controlling, under a given experimental condition(s).

Applicants state that the secondary reference, Hoch et al. fails to cure the deficiencies noted above for Handelsman et al. Hoch et al. teach a method of first isolating microbial organisms capable of metabolizing a target compound "T", but not a source compound "S", to an essential factor (Hoch et al. at column 1, lines 54-57). Specifically, the Hoch et al. method comprises: "providing a cell containing one or more genes responsible for converting a target compound to provide a

detectible signal,.., wherein said detectible signal is not produced in the presence of said source compound;.., and identifying cell that produces a said detectable signal in the presence of said source compound and the inducer of said promoter, but not in the presence of said source compound and absence of said inducer" (Hoch et al. at claim 1). This is opposite of what the present invention teaches and claims. The parallel testing method in claim 19 explicitly requires selection of cells based on cell growth which is a detectible signal, in the presence of the substrate and the product to obtain the desired phenotype (Ai+; B+).

In reply, attention is drawn to the teachings of Hoch at e.g., Example 1 which states:

> One of the isolates that could utilize AsA as its sole source of carbon and energy (i.e., reads on the claim only source of an element essential to growth), but could not grow on 2-KLG, was identified as Kelbsiella oxytoca (Table 1). Thus, Kelbsiella oxytoca was retained as a candidate for genetic engineering of a host strain that can use AsA under controlled conditions for the selection of cloned microbial pathways from 2-KLG to AsA….
> Other bacterial strains capable of metabolizing ascorbic acid to carbon and energy were also identified, as were some that also metabolized 2KLG to carbon and energy (Table 1).

Thus, for Handelsman to have successfully assayed the transformed cell would have indicated, at least implicitly, the growth of the cell in a medium containing the substrate and

product. The transformation of the substrate into the product in the transformed cell would indicate the survival of the substrate and/or product solely in the medium to result in a transformed cell. This is explicitly taught by Hoch. The combined teachings of Handleman and Hock would therefore lead one having ordinary skill in the art to the claimed method. There is nothing new and unobvious about the claim **generic** method. The biosynthetic (enzymatic) pathway of obtaining a product from a substrate in a transformed host cell under a minimum essential growth media of the substrate/product is no more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007). (This is evident from the method describe in the instant disclosure applying the general method known in the art to e.g., search for the metabolic pathway for the bioconversion of phytosterols into 4-androstene-3,17-dione (AD).)

No claim is allowed.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Minshull et al (6391640) discloses methods for cellular and metabolic engineering.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639